510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K051806

B. Purpose for Submission:

Marketing device in U.S.

C. Measurand:

Human Hemoglobin

D. Type of Test:

Fecal Occult Blood

E. Applicant:

Epitope Diagnostics, Inc.

F. Proprietary and Established Names:

CARE™ Fecal Occult Blood (FOB) Test

G. Regulatory Information:

1. Regulation section:

   21 CFR 864.6550

2. Classification:

   Class II

3. Product code:

   KHE-Reagent, Occult Blood

4. Panel:

   Hematology (81)

H. Intended Use:

1. Intended use(s):

   Epitope Diagnostics CARE™ Fecal Occult Blood Test Device is a rapid immunological test intended for the qualitative detection of fecal occult blood in feces by professional laboratories and physician office laboratories. The test is intended for the determination of gastrointestinal (GI) bleeding, found in a number of gastrointestinal disorders, e.g., diverticulitis, colitis, polyps, and colorectal cancer.

2. Indication(s) for use:

   The CARE™ Fecal Occult Blood Test Device is recommended for use in (1) routine physical examinations, (2) monitoring any bleeding in patients, and (3) screening for colorectal cancer or gastrointestinal bleeding.

3. Special conditions for use statement(s):

4. Special instrument requirements:

I. Device Description:

The CARE™ Fecal Occult Blood (FOB) kit consists of a fecal sample collection device containing and extraction buffer and an immunoassay test strip in a sealed foil pouch with desiccant.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Clearview Ultra FOB Test

2. Predicate 510(k) number(s):

   K041297

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Test Principle	Immunoassay lateral flow test strip system utilizing MAbs for the detection of human hemoglobin	Immunoassay lateral flow test strip system utilizing MAbs for the detection of human hemoglobin
Sample	Feces in an extraction buffer	Feces in an extraction buffer

Differences		
Item	Device	Predicate
Extraction Buffer	Tris buffer	HEPES buffer
Test Device	Dipstick assembled in a house	Dipstick
Indicator Color	Red	Blue

K. Standard/Guidance Document Referenced (if applicable):

"Review Criteria for the Qualitative Assessment of Fecal Occult Blood In Vitro Diagnostic Devices"

L. Test Principle:

The CARE™ Fecal Occult Blood (FOB) Test is an immunoassay utilizing two monoclonal antibodies (MAbs) to specifically detect the presence of human hemoglobin (hHb) or occult blood in feces. The dipstick test strip incorporates a membrane immobilized murine anti-Hb capture MAb and a labeled murine anti-hHb signal MAB. The procedural control region contains an immobilized goat anti-mouse IgG specific antibody. The sample end of the test strip is dipped in the fecal extract. The liquid fecal extract migrates by capillary action through the test strip. If human hemoglobin is present at a level of greater than 50 ng/mL, an immuno-complex of "labeled monoclonal anti-human hemoglobin antibody-human hemoglobin-membrane immobilized monoclonal anti-human hemoglobin antibody" is formed and a red colored band appears in the test region, which is located in the lower half of the test membrane. A same colored band must appear in the control region located in the upper half of the test membrane, indicating the test strip is working and the result is valid.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility studies were conducted at three physician office labs (POLs), 210 human hemoglobin free stool extracts were collected and separated in seven groups of twenty. Each group of specimens was spiked with a known level of human hemoglobin to result in the following concentrations; 0 ng/mL, 37.5 ng/mL, 50 ng/mL (at the cut-off), 62.5 ng/mL (just above the cut-off), and 200 ng/mL, 1,000 ng/mL, and 10,000 ng/mL (prozone). POL subjects of various degrees of educational backgrounds and experiences participated in the reproducibility studies conducted at three sites. The total number of determinations of the CARE™ test at the POLs was 210. The results of the studies are presented in the table. The number of positive and negative results for each level of spiked hemoglobin concentration is presented. There was over 99.0% (208/210) agreement between the results obtained from the POL and the results obtained from the reference laboratory. The overall accuracy of the CARE™ test by the POL users was 96.6% (203/210).

Reproducibility Studies by POL and Professional User

	Tested by Laboratory Professional User						
	Target Concentration of Hb in extracted fecal sample (ng/mL)						
	0	**37.5**	**50**	**62.5**	**200**	**1000**	**10000**
Positive reads	**0**	**4**	**27**	**30**	**30**	**30**	**30**
Negative reads	**30**	**26**	**3**	**0**	**0**	**0**	**0**
Total	**30**	**30**	**30**	**30**	**30**	**30**	**30**
	Tested by Staffs at Three Physician's Office						
	Target Concentration of Hb in extracted fecal sample (ng/mL)						
	0	**37.5**	**50**	**62.5**	**200**	**1000**	**10000**
Positive reads	**0**	**5**	**28**	**30**	**30**	**30**	**30**
Negative reads	**30**	**25**	**2**	**0**	**0**	**0**	**0**
Total	**30**	**30**	**30**	**30**	**30**	**30**	**30**

b. Linearity/assay reportable range:

No prozone effect was seen up to 100,000 ng hHb/mL

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Internal (Procedural) Control: Is built into the test strip and assures that the sample addition and migration through the test strip has occurred and that the control anti-mouse antibody and the signal

antibody are intact and functional.
External Control: Assures that the membrane immobilized and labeled signal antibodies are present and reactive. This control should be performed once per kit lot per operator.

d. Detection limit:

The analytical cut-off for the CARE FOB test is 50 ng/mL. The reproducibility data showed 91.6% of the samples tested positive at 50 ng/mL.

e. Analytical specificity:

Cross-reaction to animal blood

A performance study was completed to investigate the cross reactivity of other species of hemoglobin (HB) on the CARE FOB test HB of bovine, equine, rabbit, sheep, fish, chicken and goat origin was added to 3 vials filled with fecal sample extraction buffer to a final concentration of above 1000 ng/mL but below 100,000 ng/mL. The results showed that all of these samples were negative, which indicates that the CARE FOB test does not cross-reactive with animal blood.

Meat extracts

Ground raw meat extract from beef, pork, goat chicken, fish and rabbit were added into both negative and positive (spiked to a final concentration of hHb 62.5 ng/mL) fecal sample extracts. Six replicates of each raw meat extract were assayed with three lots of the CARE™ FOB test. The results showed that there was no interference from the meat extracts.

Human hemoglobin

Two types of abnormal blood were tested (Thalassemia and Sickle Cell) and the results compared to Normal human hemoglobin (hHb). Stool extract samples were spiked with whole human blood (approximately 12.5 g/dL hemoglobin) at four different concentrations: 0, 10, 50, and 150 ng/mL. The results showed that for all three types of hHb at the concentration of 0 and 10 ng/mL the CARE FOB test was negative and at the concentrations of 50 and 100,000 ng/mL the CARE FOB test was positive. .

Dietary substances

Aqueous extracts of raw broccoli, cauliflower, cantaloupe, horseradish, turnip and vitamin C were added into both negative and positive (spiked to a final concentration of 62.5 ng/mL) fecal extracts. The results showed there was no interference from dietary substances.

Toilet water

Toilet water was tested with the presence of various cleaners, from enzymatic to Clorox based. Toilet water was added to normal stool extracts at both 0 and 50 ng/mL human hemoglobin (hHb). All of

the 62 ng/mL Hb samples spiked with toilet water samples were positive on the CARE™ FOBT and all the 0 ng/mL Hb samples spiked with toilet water continued to be negative with CARE™ FOBT.

Contaminants

A residual concentration equal to 1000 ng/mL of Hb that remains in the toilet water will produce a false positive result when introduced to the CARE™ FOBT. It is suggested to avoid contact of the feces specimen with the toilet water during the collection process, as well as to flush the toilet bowl before sampling. It is preferable for the specimen to be collected on clean paper or in a clean container.

f. Assay cut-off:

2. Comparison studies:

a. Method comparison with predicate device:

A laboratory professional user tested the same set of extracted samples (Positive: N=150; Negative N=120) with the CARE™ FOB test and the Clearview Ultra FOB test (predicate device). There was 98.5% (296/270) agreement between the results obtained from the predicate and test device.

b. Matrix comparison:

N/A

3. Clinical studies:

a. Clinical Sensitivity:

N/A

b. Clinical specificity:

N/A

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

   N/A

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.